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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,040	08/29/2006	Friederike Hesse	22389	6496
151	7590	12/04/2008	EXAMINER	
HOFFMANN-LA ROCHE INC.			ALLEN, MARIANNE P	
PATENT LAW DEPARTMENT				
340 KINGSLAND STREET			ART UNIT	PAPER NUMBER
NUTLEY, NJ 07110			1647	
			MAIL DATE	DELIVERY MODE
			12/04/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/591,040	HESSE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Marianne P. Allen	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 09 September 2008.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-7 and 9-11 is/are rejected.

7) Claim(s) 8 is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

Applicant's arguments filed 9/9/08 have been fully considered but they are not persuasive.

The rejection of claims 1 and 3 under 35 U.S.C. 103 is withdrawn in view of the amendments to the claims. It is noted that applicant's citation for Stahl et al. in the response is incorrect. The reference is Stahl et al., Biochem. J., 1997 (reference C11, of record).

Neither Nesbit et al. nor Stahl et al. disclose SEQ ID NO: 2. Nakamura (U.S. Patent No. 6,855,685) discloses a hepatocyte growth factor NK4 fragment corresponding to SEQ ID NO: 2 except for the N-terminal methionine and the serine at amino acid position 2. (See SEQ ID NO: 1 of Nakamura.) The prior art of record does not disclose nor suggest mutating the glutamine at amino acid position 1 of SEQ ID NO: 1 of Nakamura to serine in order to improve N-terminal homogeneity when this fragment is produced in *E. coli*. (See instant specification at pages 4 and 6.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1 has been amended and claims 7-11 have been newly introduced.

Claim 1 has been amended to further define the solutions used in steps (c) and (d).

Applicant points to page 4 for basis. However, page 4 of the specification discloses:

*The inclusion bodies were solubilized by adding a denaturing agent like 6 M guanidinium hydrochloride or 8 M urea at pH 7-9 in phosphate buffer (preferably in a concentration of 0.1 - 1.0 M, e.g. 0.4 M) preferably in the presence of DTT (dithio-1,4-threitol). The solubilisate is diluted in phosphate buffer pH 7-9 in the presence of GSH/GSSG (preferably 2-20 mM glutathion) and a denaturing agent in a non denaturing concentration (e.g. 2M guanidinium hydrochloride or 4 M urea) or preferably instead of guanidinium hydrochloride or urea, arginine in a concentration of about 0.3 to 1.0 M, preferably in a concentration of about 0.7 M.*

Claim 1 does not require a denaturing agent in a non-denaturing concentration for step (d). This portion of the specification does not disclose using the phosphate buffer at pH 7-9 in the presence of GSH/GSSG without the denaturing agent in a non-denaturing concentration. With respect to claim 9, the specification combination recited (guanidinium hydrochloride and arginine) is not specifically contemplated here. With respect to claim 11, Example 2 discloses the solutions recited in the claim. However, this example is with reference to inclusion bodies from *E. coli* (see Example 1), and the claims are directed to any microbial host cell. With respect to claim 10, Example 2 discloses use of EDTA; however, this is with particular reference to the method of Example 2 and the solutions used therein. It is not generally disclosed. Claims 9-11 are broader than the originally disclosed invention.

Claim 7 recites that the steps are performed at a pH between 8 and 9. Applicant points to page 2 for basis. However, page 2, lines 20-22, discloses using a **potassium** phosphate buffer between pH 7-9, and more preferably pH 8-9. The claims are not limited to a potassium phosphate buffer and as such claim 7 is broader than the originally disclosed invention.

*Conclusion*

Claim 8 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is (571)272-0712. The examiner can normally be reached on Monday-Friday, 5:30 am - 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/  
Primary Examiner, Art Unit 1647

mpa